

IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

1. (Currently amended) A method for detecting the presence or absence of a diseased condition in a tissue, cell type or organ of an individual, comprising ~~the following steps:~~

[[a) ]]obtaining a bodily fluid sample from an ~~said~~-individual;

[[b) ]]determining an ~~the~~-amount or presence of free floating DNA that originates from a ~~said~~-tissue, cell type or organ in the ~~said~~-sample; and

[[c) ]]determining the presence or absence of a diseased condition based on the amount or presence of free floating DNA that originates from the ~~said~~-tissue, cell type or organ.

2. (Currently amended) A method for detecting the presence or absence of a diseased condition in a tissue, cell type or organ of an individual, comprising ~~the following steps:~~

[[a) ]]obtaining a bodily fluid sample from an ~~said~~-individual;

[[b) ]]determining an ~~the~~-amount of total free floating DNA in the ~~said~~-sample;

[[c) ]]determining an ~~the~~-amount of free floating DNA that originates from a particular ~~said~~ tissue, cell type or organ in the ~~said~~-sample; and

[[d) ]]determining the presence or absence of a diseased condition based on the total amount of free floating DNA and the fraction of free floating DNA that originates from the ~~said~~ tissue, cell type or organ.

3. (Currently amended) The method ~~according to~~ of any one of claims 1 and 2, ~~wherein claim 1 or 2, characterised in that~~ the sample is conditioned before the amount or presence of free floating DNA is determined.

4. (Currently amended) The method ~~according to~~ of claim 3, wherein ~~characterised in that~~ the sample is conditioned by at least one ~~means~~-of centrifugation, filtering, heating, cooling, concentration and ~~or~~-chemical treatment.

5. (Currently amended) The method of any one of claims 1 and 2, wherein ~~determining according to one of the preceding claims, characterised in that~~ the amount or presence

of DNA originating from the tissue, cell type or a certain organ or tissue is determined by comprises analysing for a DNA methylation pattern that is characteristic for the tissue, cell type or organ ~~said organ, tissue or cell type~~.

6. (Currently amended) The method of according to claim 5, wherein the ~~characterised in that said~~ methylation pattern is characteristic for the tissue, cell type or organ ~~said organ, tissue or cell type~~ and not found in other tissues, cell types or organs, ~~tissues or cell types~~ involved in the diseased ~~medical~~ condition of interest.

7. (Currently amended) The method of claim 5, wherein the diseased ~~according to any of the preceding claims, characterised in that the medical condition is~~ at least one from the group consisting of a cell proliferative and a ~~and/or~~ neoplastic disease.

8. (Currently amended) The method of claim 5, wherein the sample comprises at least one bodily fluid selected from the group consisting of ~~according to any of the preceding claims, characterised in that the samples are obtained from bodily fluids like~~ whole blood, blood plasma, blood serum, urine, sputum, ejaculate, semen, tears, sweat, saliva, lymph fluid, bronchial lavage, pleural effusion, peritoneal fluid, meningeal fluid, amniotic fluid, glandular fluid, fine needle aspirates, nipple aspirate fluid, spinal fluid, conjunctival fluid, vaginal fluid, duodenal juice, pancreatic juice, bile and cerebrospinal fluid ~~from said individual~~.

9. (Currently amended) The method of claim 5, wherein determining ~~according to one of the preceding claims, characterised in that the methylation pattern~~ comprises ~~is determined by~~ subjecting the DNA to a chemical or enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position 5-methylated cytosines unmodified.

10. (Currently amended) A method for detecting the presence or absence ~~absence or presence of a diseased condition in a tissue, cell type or organ, an organ, cell type or tissue,~~ comprising ~~performing the following steps:~~

[[a) ~~]]obtaining~~ retrieving a bodily fluid sample;

[[b) ~~]]determining~~ an ~~the~~ amount or presence of free floating DNA that exhibits a DNA

~~methylation pattern characteristic of a tissue-, cell type- or organ-tissue-, organ- or cell type-characteristic DNA methylation pattern;~~

~~[[c) ]]~~~~determining~~ ~~concluding~~, whether there is an abnormal level of free floating DNA that originates from ~~the said-tissue, cell type or organ;~~ and

~~[[d) ]]~~~~determining a presence or absence of a diseased condition associated with said tissue, cell type or organ, based on the presence or absence, respectively, of such an abnormal level of free floating DNA~~ ~~concluding, whether a diseased condition associated with said tissue, cell type or organ is absent or present.~~

11. (Currently amended) A method for detecting the ~~absence or presence~~ or absence of a diseased condition in a specific tissue, cell type or organ, ~~cell type or tissue,~~ comprising the following steps:

[[a) ]]~~obtaining~~ ~~retrieving~~ a bodily fluid sample;

[[b) ]]~~detecting an~~ ~~the~~ amount of total free floating DNA in ~~the said~~ sample;

[[c) ]]~~determining an~~ ~~the~~ amount of free floating DNA that originates from ~~a said-specific tissue, cell type or organ by determining an amount of free floating DNA that exhibits a DNA methylation pattern characteristic of a tissue-, cell type- or organ-~~ ~~exhibits a tissue-, cell type- or organ-characteristic DNA methylation pattern;~~

[[d) ]]~~determining the fraction of total free floating DNA that originates from the said specific tissue, cell type or organ;~~

[[e) ]]~~determining~~ ~~concluding~~, whether an abnormal level of free floating DNA that originates from ~~the said specific tissue, cell type or organ is present; and~~

[[f) ]]~~determining the presence or absence of a diseased condition associated with said tissue, cell type or organ, based on the presence or absence, respectively, of such an abnormal level of free floating DNA~~ ~~concluding, whether a diseased condition associated with said specific tissue, cell type or organ is absent or present.~~

12. (Currently amended) A method for determining the fraction of free floating DNA in a bodily fluid that originates from a specific tissue, cell type or ~~an organ, cell type or tissue of interest,~~ comprising the following steps:

[[a) ]]~~obtaining~~ ~~retrieving~~ a bodily fluid sample;

[[b) ]]conditioning the said sample in order to provide for allow a binding of free floating DNA to a surface;

[[c) ]]binding an amount essential fraction of the said-total free floating DNA to the said surface;

[[d) ]]detecting an the-amount of total free floating DNA by measuring the amount of DNA bound to the said-surface;

[[e) ]]subjecting the said-surface comprising the said-bound DNA to at least one of a chemical and and/or enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position-5 methylated cytosines unmodified;

[[f) ]]amplifying the treated DNA;

[[g) ]]analysing several methylation-specific positions in the said-treated DNA, and thereby determining an the-amount of DNA that exhibits a tissue, cell type or organ-characteristic DNA methylation pattern; and

[[h) ]]determining the fraction of total free floating DNA that originates from the specific said-tissue, cell type or organ.

13. (Currently amended) The method of claim 12, further comprising the following additional steps:

[[i) ]]determining whether an abnormal level of free floating DNA that originates from the said specific tissue, cell type or organ is present~~concluding, whether said DNA originates from said tissue, cell type or organ, if there is an abnormal level of total free floating DNA;~~ and

[[j) ]]determining the presence or absence of a diseased condition associated with said tissue, cell type or organ, based on the presence or absence, respectively, of such an abnormal level of free floating DNA~~concluding, whether a medical condition associated with said tissue, cell type or organ is present.~~

14. (Currently amended) The method of any one of claims 1, 2, 10, 11, 12 and 13, wherein measuring according to any of the preceding claims, characterised in that the total amount of free floating DNA comprises use of at least one means selected from the group consisting of: is ~~measured by~~ intercalating fluorescent dyes or other dyes exhibiting changing ~~their~~ fluorescence properties upon ~~when~~ binding to DNA; [[,]] hybridisation to DNA specific oligonucleotide or PNA

~~oligomer probes; including, but not limited to oligonucleotides or PNA oligomers, real time PCR assays; or other real time amplification procedures;[[,]] UV-Vis absorbance; and or in general amplification procedures with subsequent determination of the amount of product amplificate formed.~~

15. (Currently amended) A kit for determining the total amount of free floating DNA in serum, comprising:

a surface suitable to bind free floating DNA ~~floating in~~ of a sample ~~volume~~ of bodily fluid;[[,]]

[[a ]]means for detecting an ~~the~~ amount of DNA bound to the ~~this solid~~ surface;[[,]]

reagents suitable to chemically or enzymatically modify the surface bound DNA ~~bound to the surface~~ to convert all unmethylated cytosines in the DNA into uracil but leave position-5 methylated cytosines unmodified;[[,]]

a container suitable to host the surface and said reagents;[[,]] and

[[a ]]means to control and adjust the temperature in the container~~this chamber~~.